

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

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Amendments to the Claims:

APR 21 2008

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (previously presented): A multiparameter screening Method for atherosclerosis-related coronary heart disease (CHD) or stroke comprising;

defining the disease as atherosclerosis-related CHD or stroke;

defining the normal as free from said disease;

defining the following parameters as atherosclerotic parameters consisting of c = the Low-density lipoprotein (LDL) concentration parameter in mg/dL or c = the C-reactive protein (CRP) concentration parameter in mg/L, p = the blood systolic pressure parameter in mmHg or p = the blood diastolic pressure parameter in mmHg, f = the heart rate parameter in  $s^{-1}$ , a = the radius parameter along arterial radius in cm, T = the temperature parameter of blood plasma in  $^{\circ}\text{C}$ ,  $\alpha$  = the angle parameter

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

between the gravity and the mean velocity of blood fluid in arterial vessels in degree and  $z$  = the axial length parameter of diffusion flux along the inner wall in the axial direction of arterial vessels in cm, called the diffusion length parameter;

measuring, for an individual, the values of said atherosclerotic parameters presented in the following expressions:

$$J = A c^{\frac{11}{9}} (v^3 D^{16})^{\frac{1}{27}} \left( \frac{g \cos \alpha + fu}{z} \right)^{\frac{2}{9}} \quad (1.1)$$

or

$$J = B c^{\frac{11}{9}} p^{\frac{1}{3}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}} \quad (1.2)$$

and

$$J = E c^{\frac{11}{9}} D^{\frac{16}{27}} z^{-\frac{2}{9}} (\cos \alpha)^{\frac{2}{9}} \quad (1.3)$$

wherein  $J$  = the mass transfer flux in  $10^{-5}$  g/(cm<sup>2</sup>s),  $A$ ,  $B$  and  $E$  = the constants of conversion factors,  $v$  = the eddy velocity of blood fluid in arterial vessels in cm/s,  $u$  = the mean velocity of the blood fluid in cm/s,  $D$  = the diffusion coefficient in cm<sup>2</sup>/s, and  $g$  = the gravitational acceleration in cm/s<sup>2</sup>;

measuring, for an individual not having the disease, the normal values of said

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

atherosclerotic parameters;

determining the disease risks yielded by the difference between said measured values and said normal values of said atherosclerotic parameters;

adding all said disease risks containing a total risk of said disease;

determining a disease risk level containing said total risk of said disease;

selecting an atherosclerotic risk factor related to an atherosclerotic parameter having the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease;

selecting a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease;

selecting a greater concentration level between the LDL level in the serum and the CRP level in

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

the blood plasma so as to result in said greater level as a secondary therapy target of said disease;

calculating a relative ratio between currently said total risk and previously said total risk so as to yield said relative ratio as a therapeutic efficacy of said disease;

repeating above-mentioned methods until said disease risk level to reduce to a normal level for the individual who requires a therapy to prevent or to treat atherosclerosis-related CHD or stroke;

above-mentioned methods are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said methods; and

outputting said total risk, said risk level, said primary cause, said therapeutic target and said therapeutic efficiency to a user or a display.

Claim 2 (previously presented): A method as in

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

claim 1, wherein the nine disease risks are yielded by the differences between the measured values and the normal values of the nine atherosclerotic parameters, wherein:

substituting a measured value,  $Cm_1$  in mg/dL, of the individual's LDL concentration in human serum, wherein said  $Cm_1$  is determined using a medical technique for measuring the concentration of blood constituents or said  $Cm_1$  is determined by the physician, into eq. 1.1

$$\text{yields } Jm_1 = H Cm_1^{\frac{11}{9}} \text{ where } H = A(v^3 D^{16})^{\frac{1}{27}} \left( \frac{g \cos \alpha + f u}{z} \right)^{\frac{2}{9}},$$

substituting a normal value,  $Cn_1$  in mg/dL, of said LDL concentration parameter, wherein said  $Cn_1$  is determined by the physician or said  $Cn_1$  = 100 mg/dL for adult, into eq. 1.1 yields

$$Jn_1 = H Cn_1^{\frac{11}{9}},$$

calculating  $\frac{Jm_1 - Jn_1}{Jn_1}$  yields:

$$R_1 = \left( \frac{Cm_1}{Cn_1} \right)^{\frac{11}{9}} - 1 \quad (1)$$

where  $Cm_1 \geq Cn_1$ , and

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

calculating (1) yields the disease risk  $R_1$  caused by the LDL concentration parameter related to the atherosclerotic risk factors being an elevated LDL concentration in human serum, high-fat diet, hypercholesterolemia or other risk factors that increase said LDL concentration;

substituting a measured value,  $Cm_2$  in mg/L, of the individual's CRP concentration in human blood plasma, wherein said  $Cm_2$  is determined using a medical technique for measuring the concentration of blood constituents or said  $Cm_2$  is determined by the physician, into

eq. 1.1 yields  $Jm_2 = HCm_2^{\frac{11}{9}}$  where

$$H = A(v^3 D^{16})^{\frac{1}{27}} \left( \frac{g \cos \alpha + f u}{z} \right)^{\frac{2}{9}},$$

substituting a normal value,  $Cn_2$  in mg/L, of said CRP concentration parameter, wherein said  $Cn_2$  is determined by the physician or said  $Cn_2 = 1.0$  mg/L for adult, into eq. 1.1 yields

$$Jn_2 = HCn_2^{\frac{11}{9}},$$

calculating  $\frac{Jm_2 - Jn_2}{Jn_2}$  yields:

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

$$R_2 = F \left( \frac{Cm_2}{Cn_2} \right)^{\frac{11}{9}} - 1 \quad (2)$$

where  $Cm_2 \geq Cn_2$ , the equivalent factor  $F = \left( \frac{D_c}{D_L} \right)^{\frac{16}{27}}$ ,

$D_c$  = the CRP diffusion coefficient,  $D_L$  = the LDL diffusion coefficient, and

calculating (2) yields the disease risk  $R_2$  caused by the CRP concentration parameter related to the atherosclerotic risk factors being an elevated CRP level in human blood plasma, systemic inflammation, infectious agents or other risk factors that increase said CRP level;

substituting a measured value,  $Pm_3$  in mmHg, of the individual's blood systolic pressure, wherein said  $Pm_3$  is determined using a medical technique for measuring the human blood pressure or said  $Pm_3$  is determined by the physician, into eq. 1.2 yields  $Jm_3 = H_p Pm_3^{\frac{1}{3}}$  where

$$H_p = Bc^{\frac{11}{9}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}},$$

substituting a normal value,  $Pn_3$  in mmHg, of said systolic pressure parameter, wherein said  $Pn_3$  is determined by the physician or said  $Pn_3$  =

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

120 mmHg for adult, into eq. 1.2 yields

$$Jn_3 = H_p Pn_3^{\frac{1}{3}},$$

calculating  $\frac{Jm_3 - Jn_3}{Jn_3}$  yields:

$$R_3 = \left( \frac{Pm_3}{Pn_3} \right)^{\frac{1}{3}} - 1 \quad (3)$$

where  $Pm_3 \geq Pn_3$ , and

calculating (3) yields the disease risk  $R_3$  caused by the systolic pressure parameter related to the atherosclerotic risk factors being an elevated level of blood systolic pressure, family history of hypertension or other risk factors that increase said systolic pressure;

substituting a measured value,  $Pm_4$  in mmHg, of the individual's blood diastolic pressure, wherein said  $Pm_4$  is determined using a medical technique for measuring the human blood pressure or said  $Pm_4$  is determined by the physician, into eq. 1.2 yields  $Jm_4 = H_p Pm_4^{\frac{1}{3}}$  where

$$H_p = Bc^{\frac{11}{9}} T^{\frac{16}{27}} a^{\frac{2}{3}} f^{\frac{2}{9}} z^{-\frac{2}{9}},$$

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

substituting a normal value,  $Pn_4$  in mmHg, of said blood diastolic pressure parameter, wherein said  $Pn_4$  is determined by the physician or said  $Pn_4 = 70$  mmHg for adult, into eq. 1.2 yields

$$Jn_4 = H_p Pn_4^{\frac{1}{3}},$$

calculating  $\frac{Jm_4 - Jn_4}{Jn_4}$  yields:

$$R_4 = \left( \frac{Pm_4}{Pn_4} \right)^{\frac{1}{3}} - 1 \quad (4)$$

where  $Pm_4 \geq Pn_4$ , and

calculating (4) yields the disease risk  $R_4$  caused by the diastolic pressure parameter related to the atherosclerotic risk factors being an elevate level of blood diastolic pressure, family history of hypertension or other risk factors that increase said diastolic pressure;

substituting a measured value,  $Fm_5$  in  $s^{-1}$ , of the individual's heart rate, wherein said  $Fm_5$  is determined using a medical technique for measuring the human heart rate or said  $Fm_5$  is determined by the physician, into eq. 1.2 yields  $Jm_5 = H_f Fm_5^{\frac{2}{9}}$  where  $H_f = Bc^{\frac{11}{9}} T^{\frac{16}{27}} a^{\frac{2}{3}} p^{\frac{1}{3}} z^{-\frac{2}{9}}$ ,

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

substituting a normal value,  $Fn_5$  in  $s^{-1}$ , of said heart rate parameter, wherein said  $Fn_5$  is determined by the physician or said  $Fn_5 = 72$  per minute for adult, into eq. 1.2 yields

$$Jn_5 = H_f F_{n_5}^{\frac{2}{9}},$$

calculating  $\frac{Jm_5 - Jn_5}{Jm_5}$  yields:

$$R_s = \left( \frac{Fm_5}{Fn_5} \right)^{\frac{2}{9}} - 1 \quad (5)$$

where  $Fm_5 \geq Fn_5$ , and

calculating (5) yields the disease risk  $R_s$  caused by the heart rate parameter related to the atherosclerotic risk factors being an elevated level of heart rate, smoking cigarette, depression or other risk factors that increase said heart rate;

substituting a measured radius value,  $Am_6$  in cm, of the individual's arterial vessel at the lesion-prone sites of arterial bifurcations, arterial branching, arterial curvatures or arterial tapering, wherein said  $Am_6$  is determined using a medical technique for measuring the sizes of arterial vessels or said

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

$A_{m_6}$  is determined by the physician, into eq.

$$1.2 \text{ yields } J_{m_6} = H_a A_{m_6}^{\frac{2}{3}} \text{ where } H_a = B c^{\frac{11}{9}} T^{\frac{16}{27}} f^{\frac{2}{9}} p^{\frac{1}{3}} z^{-\frac{2}{9}},$$

substituting a normal value,  $A_{n_6}$  in cm, of said arterial radius parameter, wherein said  $A_{n_6}$  is determined by the physician or said  $A_{n_6} =$  a value between 0.2 cm and 2.2 cm for adult,

$$\text{into eq. 1.2 yields } J_{n_6} = H_a A_{n_6}^{\frac{2}{3}},$$

calculating  $\frac{J_{m_6} - J_{n_6}}{J_{n_6}}$  yields:

$$R_6 = \left( \frac{A_{m_6}}{A_{n_6}} \right)^{\frac{2}{3}} - 1 \quad (6)$$

where  $A_{m_6} \geq A_{n_6}$ , and

calculating (6) yields the disease risk  $R_6$  caused by the arterial radius parameter related to the atherosclerotic risk factors being an increased size of arterial radius at said lesion-prone sites or other risk factors that increase the size of said arterial radius;

substituting a measured temperature value,  $T_{m_7}$  in °C, of the individual's plasma fluid in the region at said lesion-prone sites, wherein said  $T_{m_7}$  is determined using a medical technique for

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

measuring the temperature of human blood plasma or said  $T_m$ , is determined by the physician, into eq. 1.2 yields  $J_m = H_T T_m^{\frac{16}{27}}$  where

$$H_T = B c^{\frac{11}{9}} a^{\frac{2}{3}} f^{\frac{2}{9}} p^{\frac{1}{3}} z^{-\frac{2}{9}},$$

substituting a normal value,  $T_n$ , in  $^{\circ}\text{C}$ , of said plasma temperature parameter, wherein said  $T_n$ , is determined by the physician or said  $T_n = 37^{\circ}\text{C}$ , into eq. 1.2 yields  $J_n = H_T T_n^{\frac{16}{27}}$ ,

calculating  $\frac{J_m - J_n}{J_n}$  yields:

$$R = \left( \frac{T_m}{T_n} \right)^{\frac{16}{27}} - 1 \quad (7)$$

where  $T_m \geq T_n$ , and

calculating (7) yields the disease risk  $R$ , caused by the plasma temperature parameter related to the atherosclerotic risk factors being an elevated temperature of said human blood plasma at said lesion-prone sites, elevated body temperature-related diseases or other risk factors that increase said plasma temperature;

substituting a measured value,  $\alpha_m$ , in degree, of

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

the angle between the gravity and the average velocity of the blood fluid in the region at said lesion-prone sites, wherein said  $\alpha m_8$  is determined using a medical technique for measuring the human arterial geometries or said  $\alpha m_8$  is determined by the physician, into

$$\text{eq. 1.3 yields } Jm_8 = H_a (\cos \alpha m_8)^{\frac{2}{9}} \text{ where } H_a = Ec^{\frac{11}{9}} D^{\frac{16}{27}} z^{-\frac{2}{9}},$$

substituting a normal value,  $\alpha n_8$  in degree, of said angle parameter, wherein said  $\alpha n_8$  is determined by the physician or said  $\alpha n_8 =$  a value between the  $10^\circ$  and  $60^\circ$  for adult, into  
eq. 1.3 yields  $Jn_8 = H_a (\cos \alpha n_8)^{\frac{2}{9}},$

calculating  $\frac{Jm_8 - Jn_8}{Jn_8}$  yields:

$$R_8 = \left( \frac{\cos \alpha m_8}{\cos \alpha n_8} \right)^{\frac{2}{9}} - 1 \quad (8)$$

where  $\alpha n_8 \geq \alpha m_8$ , and

calculating (8) yields the disease risk  $R_8$  caused by the angle parameter related to the atherosclerotic risk factors being a reduced size of said angle or other risk factors that reduce said angle size; and

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

substituting a measured value,  $Zm_9$  in cm, of the individual's axial length of diffusion flux along the inner arterial wall at said lesion-prone sites, wherein said  $Zm_9$  is determined using a medical technique for measuring the human arterial geometries or said  $Zm_9$  is determined by the physician, into eq. 1.1

$$\text{yields } Jm_9 = H_z Zm_9^{-\frac{2}{9}} \text{ where } H_z = A c^{\frac{11}{9}} (v^3 D^{16})^{\frac{1}{27}} (g \cos \alpha + f u)^{\frac{2}{9}},$$

substituting a normal value,  $Zn_9$  in cm, of said axial length parameter, wherein said  $Zn_9$  is determined by the physician or said  $Zn_9$  = a value between 0.10 cm and 1.00 cm, into eq. 1.1 yields  $Jn_9 = H_z Zn_9^{-\frac{2}{9}}$ ,

calculating  $\frac{Jm_9 - Jn_9}{Jn_9}$  yields:

$$R_9 = \left( \frac{Zn_9}{Zm_9} \right)^{\frac{2}{9}} - 1 \quad (9)$$

where  $Zn_9 \geq Zm_9$ , and

calculating (9) yields the disease risk  $R_9$  caused by the axial diffusion length parameter related to the atherosclerotic risk factors being a decrease in said axial length of the

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

diffusion flux or other risk factors that decrease said diffusion length.

Claim 3 (previously presented): The method of claim 2, further comprising: adding said all nine disease risks  $R_1$  to  $R_9$ , containing a total risk of said disease consisting;

a current total risk of said disease related to the currently measured values of said atherosclerotic parameters; and

a previous total risk of said disease related to the previously measured values of said atherosclerotic parameters.

Claim 4 (previously presented): The method of claim 3, further comprising: determining a disease risk level containing said total risk of said disease comprising:

dividing the disease risk level into the following seven risk sublevels:  $0.84 \geq$  first disease risk level  $\geq 0.00$ ,  $1.75 \geq$  second disease risk level  $> 0.84$ ,  $2.70 \geq$  third disease risk level  $> 1.75$ ,  $3.70 \geq$  fourth disease risk

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

level > 2.70, 4.70 ≥ fifth disease risk level > 3.70, 5.80 ≥ sixth disease risk level > 4.70 and seventh disease risk level > 5.80; and

selecting a disease risk level containing said total risk of said disease from among seven of said disease risk sublevels.

Claim 5 (previously presented): The method of claim 3, further comprising: selecting an atherosclerotic risk factor related to the atherosclerotic parameter having the greatest contribution to said total risk of said disease so as to result in said risk factor as a primary therapy target of said disease.

Claim 6 (previously presented): The method of claim 2, further comprising: selecting a greater flux between the LDL mass transfer flux and the monocyte mass transfer flux so as to result in said greater flux as a primary cause in said disease comprising:

selecting the LDL mass transfer flux as a primary cause in said disease when said  $R_1 \geq$  said  $R_2$ ;  
or

selecting the monocyte mass transfer flux as a

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

primary cause in said disease when said  $R_1 <$  said  $R_2$ .

Claim 7 (previously presented): The method of claim 2, further comprising: selecting a greater concentration level between the LDL level in the human serum and the CRP level in the human blood plasma so as to result in said greater level as a secondary therapy target comprising:

selecting the LDL level in the serum as a secondary therapy target of said disease when said  $R_1 \geq$  said  $R_2$ ; or

selecting the CRP level in the plasma as a secondary therapy target of said disease when said  $R_1 <$  said  $R_2$ .

Claim 8 (previously presented): The method of claim 3, further comprising: calculating a relative ratio between said current total risk of said disease and said previous total risk of said disease so as to yield said relative ratio as a therapeutic efficacy of said disease.

Claim 9 (currently amended): The method of claim 1, further comprising: said method containing the

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

steps of:

the step 1 of calculating  $R_1 = \left(\frac{Cm_1}{Cn_1}\right)^{\frac{11}{9}} - 1$  yields the

disease risk  $R_1$  wherein  $Cm_1$  is a measured value of the individual's LDL concentration in human serum,  $Cn_1$  is a normal value of the LDL concentration parameter and  $Cm_1 \geq Cn_1$ ;

calculating  $R_2 = F \left(\left(\frac{Cm_2}{Cn_2}\right)^{\frac{11}{9}} - 1\right)$  yields the disease

risk  $R_2$  wherein  $Cm_2$  is a measured value of the individual's CRP concentration in human blood plasma,  $Cn_2$  is a normal value of the CRP

concentration parameter,  $F = \left(\frac{D_c}{D_L}\right)^{\frac{16}{27}}$ ,  $D_c$  = the CRP

diffusion coefficient,  $D_L$  = the LDL diffusion coefficient and  $Cm_2 \geq Cn_2$ ; calculating

$R_3 = \left(\frac{Pm_3}{Pn_3}\right)^{\frac{1}{3}} - 1$  yields the disease risk  $R_3$  wherein

$Pm_3$  is a measured value of the individual's blood systolic pressure,  $Pn_3$  is a normal value of the blood systolic pressure parameter and

$Pm_3 \geq Pn_3$ ; calculating  $R_4 = \left(\frac{Pm_4}{Pn_4}\right)^{\frac{1}{3}} - 1$  yields the

disease risk  $R_4$  wherein  $Pm_4$  is a measured value of the individual's blood diastolic pressure,  $Pn_4$

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

is a normal value of the blood diastolic pressure parameter and  $Pm_4 \geq Pn_4$ ; calculating

$$R_5 = \left( \frac{Fm_5}{Fn_5} \right)^{\frac{2}{9}} - 1 \text{ yields disease risk } R_5 \text{ wherein } Fm_5$$

is a measured value of the individual's heart rate,  $Fn_5$  is a normal value of the heart rate parameter and  $Fm_5 \geq Fn_5$ ; calculating

$$R_6 = \left( \frac{Am_6}{An_6} \right)^{\frac{2}{3}} - 1 \text{ yields disease risk } R_6 \text{ wherein } Am_6$$

is a measured radius value of the individual's arterial vessel at the lesion-prone sites of arterial bifurcations, arterial branching, arterial curvatures or arterial tapering,  $An_6$  is a normal value of said arterial radius parameter and  $Am_6 \geq An_6$ ; calculating

$$R_7 = \left( \frac{Tm_7}{Tn_7} \right)^{\frac{16}{27}} - 1 \text{ yields the disease risk } R_7 \text{ wherein}$$

$Tm_7$  is a measured temperature value of the individual's plasma fluid in the region at said lesion-prone sites,  $Tn_7$  is a normal value of said plasma temperature parameter and  $Tm_7 \geq Tn_7$ ;

$$\text{calculating } R_8 = \left( \frac{\cos\alpha m_8}{\cos\alpha n_8} \right)^{\frac{2}{9}} - 1 \text{ yields disease risk } R_8 \text{ wherein } \alpha m_8$$

is a measured value of the angle between the gravity and the average velocity of the blood fluid in the region at said lesion-

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

prone sites,  $\alpha_{n_9}$  is a normal value of the angle parameter and  $\alpha_{n_9} \geq \alpha_{m_9}$ ; and calculating

$$R_9 = \left( \frac{Z_{n_9}}{Z_{m_9}} \right)^{\frac{2}{9}} - 1$$
 yields disease risk  $R_9$ , wherein  $Z_{m_9}$

is a measured value of the individual's axial length of diffusion flux along the inner arterial wall at said lesion-prone sites,  $Z_{n_9}$  is a normal value of said axial diffusion length parameter and  $J_{n_9} \geq J_{m_9}$ ;

the step 2 of adding all nine disease risks  $R_1$  to  $R_9$  in the step 1 containing a total risk of said disease consisting of a current total risk of said disease related to the currently measured values of the atherosclerotic parameters and a previous total risk of said disease related to the previously measured values of the atherosclerotic parameters;

the step 3 of selecting a disease risk level containing said total risk of said disease in the step 2 from following among seven of the disease risk sublevels:  $0.84 \geq$  first disease risk level  $\geq 0.00$ ,  $1.75 \geq$  second disease risk level  $> 0.84$ ,  $2.70 \geq$  third disease risk level  $> 1.75$ ,  $3.70 \geq$  fourth disease risk level  $> 2.70$ ,

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

4.70 ≥ fifth disease risk level > 3.70, 5.80 ≥ sixth disease risk level > 4.70 and seventh disease risk level > 5.80;

the step 4 of selecting an atherosclerotic risk factor related to an atherosclerotic parameter having the greatest contribution to said total risk of said disease in the step 2 so as to result in said risk factor as a primary therapy target of said disease;

the step 5 of selecting the LDL mass transfer flux as a primary cause in said disease when said R<sub>1</sub> in the step 1 ≥ said R<sub>2</sub> in the step 1 or selecting the monocyte mass transfer flux as a primary cause in said disease when said R<sub>1</sub> < said R<sub>2</sub>;

the step 6 of selecting the LDL level in human serum as a secondary therapy target of said disease when said R<sub>1</sub> in the step 1 ≥ said R<sub>2</sub> in the step 1 or selecting the CRP level in human blood plasma as a secondary therapy target of said disease when said R<sub>1</sub> < said R<sub>2</sub>; and

the step 7 of calculating a relative ratio between said current total risk of said disease

Appl. No. 10/810,296  
Dated April 19, 2008

Reply to Notice of Allowability of April 16, 2008

in the step 2 and said previous total risk of said disease in the step 2 so as to yield said relative ratio as a therapeutic efficacy of said disease; and

wherein the step 1 through the step 7 are written as an executable computer program named the MMA.exe, or another name, to be installed into a general purpose digital computer device to accomplish said method and to output a result of said method to a display or to a user comprising:

starting the MMA.exe program on said device;

inputting the currently measured values, the previously measured values and the normal values of the individual's atherosclerosis parameters into the input screen of said MMA.exe by using the keyboard of said device;

clicking the "update" button and the "calc. risk" button of said input screen;

clicking the "evaluate" button of the MMA.exe output screen; and

Appl. No. 10/810,296  
Dated April 19, 2008

**Reply to Notice of Allowability of April 16, 2008**

Claim 10 (previously presented): The method of claim 9, further comprising: repeating said method accomplished by using said device until the individual's disease risk level to reduce to a normal level for the individual who requires a therapy to prevent or to treat atherosclerosis-related CHD or stroke.